IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	)	
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HOOK et al.	)	Examiner: L. Lee
	)	
Serial No.: 09/010,317	)	Art Unit: 1645
	)	
Filed: January 21, 1998	)	Atty Docket: P06338US1/BAS

For: FIBRONECTIN BINDING PROTEIN COMPOSITIONS AND METHODS OF USE

DECLARATION UNDER 37 C.F.R. § 1.132

I, Dr. Joseph Patti, Ph.D., declare and state as follows:

1. I am one of the inventors of the above-identified patent application, and I am currently the Vice President of Clinical Research for Inhibitex, a company that specializes in products and research regarding extracellular matrix proteins including those embodied in the present invention. In addition to being a co-inventor of numerous US Patents in this field, including most recently U.S. Pat. No. 6,288,214 for Collagen Binding Protein Compositions and Methods of Use, I have also authored or co-authored numerous journal articles in this field. I am thus well familiar with the subject matter of the present invention.

2. The present invention was developed to overcome previous problems in the field of alternatives to antibiotic treatment of bacterial infection, specifically the attempt to generate antibodies to the fibronectin-binding protein which would be suitable for use in non-antibiotic methods of treating or preventing bacterial infection. Bacterial adherence and the ability of bacteria to infect host organisms have been shown to be highly related to a series of microbial adhesins which recognize and can bind to components on the extracellular matrix of host cells. One such microbial adhesin is a bacterial protein or "MSCRAMM" which has been observed to bind to the protein fibronectin ("Fn"), and

studies of the amino acid sequence of this protein indicated that there is a particular region, or fibronectin binding domain, that is primarily responsible for the ability of this MSCRAMM to bind to fibronectin. The main problem in the prior art, however, is that no one had successfully been able to develop high affinity antibodies that could block binding of bacteria such as *Staphylococcus aureus* to fibronectin. For example, when rabbit polyclonal antibodies were generated to both a recombinant form of *S. aureus* Fn-binding MSCRAMM rFnBD-D and to the Fn-binding synthetic peptide D2, a motif in a high affinity Fn-binding domain, the resulting IgG from the immune sera did not inhibit the binding of *S. aureus* to Fn. Others disclosing monoclonal antibodies raised to other motifs in the fibronectin binding domain, such as Burnham (WO 94/18327) who reported monoclonal antibodies to the native D1-D4 protein sequence, could not show the inhibitory activity of such antibodies. In light of the growing problem of antibiotic resistance, methods such as those involving antibodies to MSCRAMM's such as fibronectin are of extreme importance, and the ability to develop antibodies which can prevent the binding of fibronectin binding proteins to fibronectin has been a long-sought, but previously unobtainable goal prior to the present invention.

3. As a result of our efforts to overcome the drawbacks of the prior art, the present inventive group was successful in developing antibodies that were able to block the binding of fibronectin to fibronectin binding proteins. The basic and novel characteristic of the invention, as set forth in great detail in Applicants' specification, is that these antibodies are raised against peptides which, while they are based upon epitopes from the fibronectin

binding domain of fibronectin binding proteins, do not themselves bind to fibronectin. This basic and novel characteristic of the present invention was so different than any other concept in this field that, despite the fact that there have been numerous articles and patent references dealing specifically with fibronectin binding proteins and epitopes therefrom, not a single article or patent reference has disclosed or suggested the basic and novel characteristic of utilizing a peptide that does not bind to fibronectin so as to generate antibodies which are useful in inhibiting binding of the fibronectin binding protein to fibronectin. The success of our group in developing novel antibodies which, unlike any of the prior art cited by the Examiner, were able to inhibit binding of the fibronectin binding protein to fibronectin has been repeatedly shown, e.g., in Examples disclosed in the present specification, such as Example 5.3.2 at page 95.

4. It is thus the case that the invention as presently claimed is clearly based on the basic and novel properties of generating an antibody to inhibit fibronectin binding proteins from binding to fibronectin that is raised to those peptides in the fibronectin binding domain which do not themselves bind to fibronectin, and these basic and novel properties are clearly indicated repeatedly throughout the specification of the above application (see, e.g., Page 8, lines 13-22; Page 9, lines 3-9, etc.) Accordingly, the Examiner's contention that the specification of the present application did not include a clear indication of the basic and novel characteristics is entirely in error. To the contrary, this novel and basic property of the present invention is repeatedly set forth in the specification as shown above, and is thus clearly indicated in the specification of the present application.

I hereby state that all statements made herein based on my own personal knowledge are true and correct and that all statements based on my information and belief are true and correct to the best of my knowledge, and further that all of these statements have been made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

9-19-01
Date

Joseph M. Patti
Dr. Joseph M. Patti, Ph.D.